University of Alberta

Digit ratio and personality: An organizational explanation for behavioral variation

by

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A thesis submitted to the faculty of Graduate Studies and Research in partial fulfillment of the requirement for the degree of Master of Science

Department of Psychology

Edmonton, Alberta

Fall, 2005

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Abstract

Testosterone is thought to organize a portion of the variability seen in two sexually dimorphic human personality traits: aggression and depression. Smaller, more masculine digit ratios (2D:4D) are associated with higher prenatal testosterone levels, greater sensitivity to androgens, or both. Austin et al. (2002) proposed that sexually dimorphic traits organized by prenatal androgens should correlate with digit ratio within each sex. I found digit ratio to correlate negatively with the propensity to engage in aggressive behavior and positively with trait depression in men. These results are consistent with the hypothesis that a portion of the variation in both aggression and depression in men are due to the organizational effects of sex hormones. In addition, I found large digit ratio differences between inbred mouse strains, and suggest that they are a promising system for investigating the correlation between digit ratio and behavioral traits.

Acknowledgments

Research funding by NIH Grant (R01 AA12714) to D. Wahlsten & NSERC (Canada) Discovery Grant (249685, 45825) to P. Hurd & D. Wahlsten respectively. I wish to thank Norman Brown, Peter Lee, Martin Daily, Jamie Dyce, Ray Engeszer, Alinda Friedman, Chris Sturdy, Bob Trivers, Thomas Udhe, Paul Vasey, Paul J. Watson, and Margo Wilson for valuable discussion and comments on the manuscript. I also wish to thank Alisha Brown, Sean Cooper, Patricia Gongal, Tricia Lowrey, Sarrah Mohamedbhai, Brandy Moisan, and Walter Espinoza for assistance in collecting the data.

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CHAPTER 1

Introduction

Aggression is an essential part of male-male competition in many species. Aggressive behaviors allow individuals to compete for limited resources, such as territories, mates, increased social status, and food, and should therefore be under strong evolutionary selection (Becker et al., 1992). Males are typically the more aggressive sex and show more intra-sexual variation in aggressive behaviors (Archer, 1988; Bakker, 1986; Holder et al., 1991; Oliveira, 1998; Salmivalli & Kaukiainen, 2004; vom Saal, 1983a). Four parallel approaches can be used to understand why a particular behavior, in this case aggression, exists. These approaches, ultimate, proximate, ontogenetic, and phylogenetic (Tinbergen, 1963), are complimentary to each other and any one approach provides only a superficial understanding of the behavior in question. I will use three of these approaches, ultimate, proximate, and ontogenetic, to examine natural variation seen in aggressive behavior.

I. Individual Variation of Aggressive Behavior

Individuals within a population vary in their propensity towards aggressive behavior (Bakker, 1986; Benus, et al., 1991). Propensity towards aggression in humans is a personality trait (an inherent personality factor that is stable over time and persists regardless of the individual's age or circumstances e.g. intelligence; Olweus, 1979; Anderson & Bushman, 2002) that predicts future aggressive acts (Bushman & Wells, 1998).

a. Ultimate causes of individual variation in aggressive behavior

While increased aggression may help an individual secure higher dominance, more territory and mates, more aggression may not always be better for an individual; too much aggression might be detrimental to the individual rather than reproductively

beneficial. Variation in aggressive behavior affects reproductive success, most likely in a non-linear fashion. We may expect an ideal or optimal level of aggression that maximizes individual fitness (Krebs & McCleery, 1984). Using this model, the variation between individuals in aggressive behavior is noise, as individuals try to balance the reproductive benefits (territories, dominance, and mates) and detrimental costs (energetic costs, injury, and death) to achieve the one optimal level of aggression (Haller, 1995; Neat et al., 1998).

An alternative view suggests different individuals use different strategies, each with a different optimal level of aggressiveness. Given the constraints imposed from genes and the environment, each male must choose one of several alternate strategies to maximize reproductive success (Frankino & Pfennig, 2001; Gross, 1996; Repka & Gross, 1995). For example, males that are larger, or healthier are able to maintain and defend territories, through aggression and dominance, thereby attracting females, while other males choose a less aggressive strategy (e.g. copulating with females on other males' territories; Rasotto & Mazzoldi, 2002; Sinervo & Lively, 1996). Behavioral alternatives allow individuals to make the most, or the best, of their inherent differences to maximize reproductive success.

b. Proximate hormonal causes of individual variation in human aggression

Males typically exhibit more aggression than females (Salmivalli & Kaukiainen, 2004; vom Saal, 1983a). Due to the sexually dimorphic nature of aggression, scientists have thought that sex hormones, such as testosterone, are responsible for variation in aggressive behavior. It is popularly believed that increased levels of circulating testosterone trigger increased levels of aggressive behavior. Many studies have searched

for such an activational effect; however, meta-analyses show only a small effect, if any at all (Archer et al., 1998; Book et al., 2001). While frequently implied, no conclusive evidence exists to support such a causal model of adult testosterone on aggressive behavior (review in Mazur and Booth, 1998). Experimental manipulations of testosterone within normal physiological ranges do not seem to have an effect on aggressive behavior (Sapolsky, 1997; Harris, 1999). Subjects exposed to supraphysiologic levels of testosterone sometimes showed increased aggression (Kouri et al., 1995) and sometimes not (Bhasin et al., 1996).

The relationship between adult hormones and aggressive behavior appears to be reciprocal rather than uni-directional (Mazur, 1983; Mazur and Booth, 1998). While testosterone influences behavior, an individual's behavior certainly influences an individual's hormones. Testosterone rises in preparation for an upcoming aggressive encounter and then increases in winners and decreases in losers (Mazur et al., 1992; Mazur and Booth, 1998). Aggression and competition have been found to affect testosterone levels in primates (Bernstein et al., 1983; Monaghan and Glickman, 1992), birds (Wingfield et al., 1987), lizards (Knapp and Moore, 1996; Yang and Wilczynski, 2002), squirrels (Buck and Barnes, 2003), fish (Hannes et al., 1984), and humans (Booth et al., 1989; Glaude et al., 1989; McCaul et al., 1992; Mazur et al., 1992; Mazur and Booth, 1998). Even vicarious aggression, such as watching aggressive acts or competitions, can raise testosterone levels in spectators (Bernhardt et al., 1998; Oliveira et al., 2001). In summary, aggressive experience has an equal if not greater effect on androgen concentrations than androgens have on aggressive behavior (Knapp and Moore, 1996; Sapolsky, 1997; Winkler and Wade, 1998).

c. Ontogenetic hormonal causes of variation in aggression

Animal models show that prenatal testosterone exposure has profound organizational effects on variation of adult aggressive behaviors (e.g. vom Saal & Bronson, 1980; Thompson & Moore, 1992; Hews et al., 1994). Male tree lizards (*Urosaurus ornatus*) differ in the exhibition of aggressive and courtship behaviors as adults and in the ability to hold territories (Hover, 1985; Moore et al., 1998). Males with orange-blue dewlaps are territorial, more aggressive, and heavier than those males with orange dewlap phenotypes (Thompson & Moore, 1992). These two fixed male phenotypes do not significantly differ in adult androgen levels (Knapp & Moore, 1995; Moore et al., 1998; Thompson & Moore, 1992); however, they appear to differ in the amount of testosterone they are exposed to during early development. Developmental hormone concentrations are hypothesized to permanently organize adult morphology and behaviors and lead to variation in individual strategies to maximize fitness in this species.

A similar organizational effect is also seen in rodents (vom Saal, 1979). Position within the uterine horn causes natural variation of androgen exposure. The term intrauterine position (IUP) refers to an individual's placement in the uterine horn with respect to the sex of an individual's neighbors, which has an effect on prenatal androgen exposure that influences individual behavior and morphology (review in Ryan & Vandenbergh, 2002; Vandenbergh, 2003). Individuals located between two males (2M) are exposed to higher concentrations of organizational testosterone than individuals located between two females (0M) because androgens produced from the neighboring males diffuse through the amniotic fluid (Clark & Galef, 1995; vom Saal & Dhar, 1992;

Vandenbergh, 2003). Female 2M mice are more aggressive (Gandelman et al., 1977; Palanza et al., 1995; Quadagno et al., 1987; Rines & vom Saal, 1984), show more novelty seeking behaviors (Vandenbergh, 2003), are more likely to mount other females (Quadagno et al., 1987; Rines & vom Saal, 1984), have larger home ranges (Zielinski et al., 1992), give birth to more male offspring (Vandenbergh & Huggett, 1995), have more fetal testosterone (vom Saal et al., 1990) and are more sensitive to testosterone (Gandelman et al., 1977) than 0M females. Male 2M mice are also more aggressive (Drickamer, 1996), exhibit more novelty seeking behaviors (Palanza et al., 2001), have larger home ranges (Drickamer, 1996), exhibit more parental behavior (vom Saal, 1983b), and are more sensitive to testosterone than 0M males (Ryan & Vandenbergh, 2002). While increased androgen exposure organizes increased aggression in mice (vom Saal, 1979), androgen receptivity increases the amount of rough and tumble play in both male and female juvenile rats (Vandenberg, 2003).

Human fraternal twins also appear to show masculinizing hormonal influences on behavior similar to the IUP effects seen in rodents. Females that share a womb with a male fraternal twin report more disinhibition, new experience seeking, and overall sensation seeking, than females with female fraternal twins (Resnick et al., 1993). An alternative explanation is the associated confound of being raised with the co-twin, which might have a sibling sex influence on an individuals' behavior through learning rather than from exposure to prenatal hormones (Resnick et al., 1993).

Other human studies have looked at variation of behavior in individuals exposed to excessive exogenous and endogenous androgens in-utero. It was once common during the mid-twentieth century to treat pregnant women at high risk of spontaneous abortion

with progestins and estrogens. As children, both males and females exposed to these androgenizing hormones in the womb were more likely to respond aggressively to conflict than their sibling controls (Reinisch, 1981). Behavior is also affected in individuals with the disease congenital adrenal hyperplasia (CAH), which causes the production of excess endogenous androgens from early in gestation to the early neonatal period (Berenbaum & Reinisch, 1997; Berenbaum et al., 2000). Females with CAH have higher levels of aggression than controls (Berenbaum & Resnick, 1997) are prone to more male typical activities and careers (Berenbaum, 1999), and exhibit masculinized sexual behavior (Hines et al., 2004). These studies demonstrate an organizational role of androgens on aggressive behavior similar to animal models; however, they lack the ability to measure how natural variations (within standard physiological ranges) in androgen concentrations contribute to variation in adult behavior.

II. Individual Variation of Morphology Due to Ontogenetic Influences

In addition to affecting behaviors, variations in prenatal hormones also effect individuals' morphologies.

a. *Anogenital Distance (AGD)*

The most salient morphological reflection of prenatal androgens in mice is ano-genital distance (AGD; Cantoni et al., 1999; Ryan & Vandenbergh, 2003). The distance between the anus and genitals is longest in males and shortest in 0M females, with 2M females showing intermediate lengths (Gandelman et al., 1977; Palanza et al., 1995; Vandenbergh, 2002). Anogenital distance is a standard, non-invasive way for scientists to identify an individual's intrauterine position, which reflects the amount of prenatal androgen exposure (Ryan & Vandenberg, 2002; Vandenbergh, 2003). Longer, more

masculine AGD, has been shown to correlate with more masculinized behaviors in both male and female mice (Cantoni et al., 1999; Drickamer, 1996; Gandelman et al., 1977; Ryan & Vandenbergh, 2002).

b. *Digit ratio (2D:4D)*

Digit ratio (2D:4D; the length of the index finger divided by the length of the ring finger) has become a popular morphological measure of the organizational influence of androgens in humans (Manning, 2002a). Since the late 1800's researchers have found digit ratio to be a sexually dimorphic trait, with a greater proportion of men having longer ring than index fingers (i.e. smaller digit ratios) than women (for a review see Peters et al., 2002). The length of the ring finger relative to the length of the index finger varies considerably between individuals in human populations (Phelps, 1952). Ecker (1875) reported three phenotypic variations in digit ratio: index shorter than ring, index longer than ring, and index equal to ring (Phelps, 1952). While all three forms have been found in both sexes, males most commonly have shorter index compared to ring fingers, while females typically exhibit a reverse pattern with longer index relative to ring fingers (George, 1930; Phelps, 1952). Of all possible digit combinations, 2D:4D remains the most dimorphic between the sexes (McFadden & Schubel, 2002). This dimorphism is stronger on the right hand, regardless of an individual's handedness (Benderlioglu & Nelson, 2004; Brown et al., 2002b; Lippa, 2003; Manning et al., 1998; McFadden & Schubel, 2002; Putz et al., 2004; Williams et al., 2000) and exists across a wide variety of populations (Manning et al., 2000; Manning et al., 2003c; Peters et al., 2002).

Digit ratio is thought to be fixed during fetal development (although the exact timing is unknown) and remain stable thereafter, even throughout puberty (Brown et al.,

2002a; Garn et al., 1975; Manning, 2002a; Manning et al., 1998). Sexual differences in 2D:4D have been shown in human digit ratio as early as 2 years of age (Manning et al., 1998). Males consistently have significantly lower digit ratios than females regardless of ethnicity; however, different ethnic groups have different average digit ratios and different degrees of sexual dimorphism (Manning et al., 2000a; Manning et al., 2003c; Peters et al., 2002). Sexual dimorphism of digit ratio in human hands is always in the same direction when it exists (Manning, 2002a; Manning et al., 2000).

Digit ratio also differs between the sexes in other species. Male adult rats have significantly lower digit ratios on their right forepaws (McMechan et al., 2004), while male adult and prepubescent mice have lower digit ratios on their hind paws (Brown, et al., 2002a; Manning et al., 2003b) than females. Digit ratio sexual dimorphism is seen in the opposite direction in zebra finch feet (Burley & Foster, 2004) and Guinea baboon hands (Roney et al., 2004). Human toes also show a trend towards this pattern of "reverse" sexual dimorphism (McFadden & Schubel, 2002).

Digit ratio is believed to reflect developmental androgen exposure in the same way that AGD does in female mice. Evidence to support this comes from individuals with congenital adrenal hyperplasia. Both males and females with elevated endogenous fetal androgens due to CAH exhibit lower, more masculine, digit ratios than controls (Brown et al., 2002c; Okten et al., 2002; but see Buck et al., 2003). Children with normal androgen levels also have digit ratios that reflect the fetal hormonal environment. Lutchmaya et al. (2004) found that male and female children with lower, more masculine digit ratios had higher fetal testosterone to estradiol ratios in amniocentesis samples than

individuals with higher ratios. These studies indicate that digit ratio reflects variation in exposure to fetal environmental androgens.

Two, non-exclusive mechanisms have been posited to explain the association between prenatal androgens and digit ratio. The first is a set of highly conserved genes (*Hoxa* and *Hoxd*) that influence the growth and patterning of the appendicular skeleton, which includes digit formation and gonad differentiation (Kondo et al., 1997; Peichel et al., 1997). Manning et al. (1998) proposed that the timing of gene regulation leaves digit ratios that reflect the quantity of fetal androgens produced. Secondly different alleles of the androgen receptor gene create natural variation in androgen sensitivity. Individuals with more CAG base pair triplet repeats in the terminal domain of the androgen receptor gene have lower sensitivity to androgens (Chamberlain et al., 1994; Kazemi-Esfarjani et al., 1995). In men, lower digit ratios are associated with fewer CAG repeats (Manning et al., 2003a), indicating that a lower digit ratio reflects greater sensitivity to androgens.

III. Digit Ratio Explains Individual Variation of Behavior

Sexual dimorphism exists for a variety of cognitive, personality, and behavioral traits, just as it does for morphological traits such as digit ratio. Austin et al. (2002) hypothesized that if a particular sexually dimorphic behavior is organized by testosterone, then digit ratio should correlate with that behavior within each sex (this will be referred to as the androgenization of trait dimorphism (ATD) hypothesis). Testosterone has been shown to organize sexually dimorphic adult reproductive and competitive behaviors (Berenbaum et al., 2000; Moore et al., 1998; Reinisch, 1981; Resnick et al., 1993; Ryan & Vandenbergh, 2002); therefore, the variation in digit ratio should reflect the degree of masculinization for these behaviors (Austin et al., 2002).

Sexual orientation is the most widely studied trait associated with digit ratio. Williams et al. (2000) hypothesized that homosexual men exhibit hyper-androgenization because they display hyper-masculine characteristics such as increased sexual partners, larger genitalia, and increased levels of circulating androgens. Both male and female homosexuals have lower, more masculine, digit ratios than heterosexuals (Hall & Love, 2003; Robinson & Manning, 2000; Rahman & Wilson, 2003; Williams et al., 2000; but see Lippa, 2003). Males with lower digit ratios, regardless of sexuality, are also perceived as more masculine and dominant by female observers (Neave et al., 2003), are more physically competitive, quicker, and generally better at sports (Manning & Taylor, 2001; Manning, 2002a; Manning, 2002b). Females with lower digit ratios, regardless of sexuality, perceive themselves as having a more masculine sex-role identity (Brown et al., 2002b; Csatho et al., 2003a), describe themselves as more competitive and assertive (Wilson, 1983), and when provoked, exhibit more reactive aggression than females with more feminine digit ratios (Benderlioglu & Nelson, 2004). Physical aggression, which is associated with male-male competition and is sexually dimorphic, should also show a relationship with digit ratio.

The second chapter tests whether natural variation in prenatal testosterone, as measured by digit ratio, permanently organizes four types of trait aggression, as predicted by the ATD hypothesis.

All the traits mentioned above suggest a competitive benefit to higher levels of prenatal testosterone. Evolutionary theory suggests that there ought to be stabilizing costs to counterbalance these benefits. Some studies find potential costs associated with higher levels of prenatal androgens, while other studies find evidence to the contrary. Autism,

hyperactivity, poor social cognition, immune deficiency and obesity are all associated with lower digit ratios, or increased exposure to prenatal testosterone (Manning et al., 2001a; Manning et al., 2001b; Manning et al., 2004; McIntyre et al., 2003; Williams et al., 2003). Conversely, individuals with more feminine digit patterns or lower prenatal testosterone are more prone to schizophrenia, emotionality, and heart attacks (Arato et al., 2004; Manning & Bundred, 2001; Williams et al., 2003). Martin et al. (1999) proposed that depression should be associated with higher levels of prenatal testosterone; however, this proposed relationship runs counter to the ATD hypothesis. Like aggression, depression is a sexually dimorphic personality trait, but unlike aggression, it is females who report more depression. We therefore expect higher levels of depression to correlate with more feminine digit ratios within each sex if depression is organized during development by prenatal testosterone.

The third chapter tests the direction of the association between depression and digit ratio (i.e. whether the direction of the correlation runs in agreement with the ATD hypothesis or that hypothesized by Martin et al.).

The ATD hypothesis may also be applied to the relationship between behavior and digit ratio in animal models. The fourth chapter examines whether inbred mouse strains exhibit sexually dimorphic digit patterns similar to those found in humans. We hypothesized that if strain or sexual dimorphism existed it should correlate with masculine behaviors, such as aggression, within sex and/or strain.

Finally, the last chapter explains the significance of the current results, and associated limitations of these results, and suggests future directions of digit ratio research.

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CHAPTER 2

Finger length ratio (2D:4D) correlates with physical aggression in men but not in women

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Published in *Biological Psychology*

Finger length ratio (2D:4D) is a sexually dimorphic trait. The ratio of second digit (index finger) to fourth digit (ring finger) is smaller for males than females in humans, mice, and baboons (Brown et al., 2002b; Manning, 2002a; Manning et al., 2000; McFadden & Bracht, 2003; McFadden & Shubel, 2002; Peters et al., 2002). In zebra finches, the sexual dimorphism in digit ratio is reversed, and males have relatively longer second digits (Burley & Foster, 2004). This reversed foot pattern matches the reversed toe 2D:4D sexual dimorphism seen in humans (McFadden & Shubel, 2002) but not that found in mice, where sexual dimorphism in hind digit ratio is in the same direction as in the human hand (Manning et al, 2003b). Sexual dimorphism in digit ratio is seen by the age of two and is thought to be stable thereafter, even through puberty (Manning et al., 1998; Brown et al., 2002b; Manning, 2002a). Index to ring finger, or 2D:4D is the most strongly dimorphic of all human digit ratio combinations (McFadden & Shubel, 2002).

Variation in finger length ratio (2D:4D) is thought to reflect the influence of prenatal testosterone during development (Manning, 2002a; Manning et al., 2003a). While this correlation is somewhat conjectural, two non-exclusive causes have been posited. The first is that common genes (Hoxa and Hoxd) underlie development of both fingers and gonads (Kondo et al., 1997; Peichel et al., 1997). The second is that allelic variation in androgen receptor sensitivity influences digit ratio. More masculine finger ratios are associated with androgen receptor alleles with fewer CAG base-pair microsatellite repeats in the terminal domain (Manning et al., 2003a). Increased number of such repeats produces receptors with lower androgen sensitivity (Chamberlain et al., 1994; Kazemi-Esfarjani et al., 1995).

More evidence for a relationship between androgen concentration during development and finger ratio comes from children with congenital adrenal hyperplasia (CAH). CAH causes the individual to be exposed to increased levels of androgens from early in gestation to the early neonatal period (Berenbaum and Reinisch, 1997). Both males and females with CAH, and therefore high developmental androgens, exhibit more masculine finger length ratios than controls (Brown et al., 2002c; Okten et al., 2002), but not necessarily when measured on the left hand (Buck et al., 2003).

Digit ratio has consistently been shown to be more dimorphic on the right hand than on the left in humans (Manning et al., 1998; McFadden & Shubel, 2002; Williams et al., 2000), baboons (McFadden & Bracht, 2003) mice (Brown et al., 2002b), and finches (Burley & Foster, 2004). Several authors have suggested that androgenization affects the right hand more than the left (McFadden & Shubel, 2002; Williams et al., 2000; Brown et al., 2002b). When both right and left hand digit ratios have been used to investigate relationships between digit ratio and psychological factors, stronger effects are seen on the right hand, or found on the right hand only (Williams et al., 2000; Brown et al., 2002a; Csatho et al., 2003a, 2003b).

Digit ratio has been shown to correlate with several psychological traits. Women with smaller digit ratios report higher, more masculinized scores on the Bem Sex Role Inventory (Csatho et al., 2003a). Men with smaller 2D:4D ratios are perceived as being more masculine and dominant by female observers (Neave et al., 2003). Manning and colleagues have found significant correlations between more masculine (small) digit ratios and achievement, ability, and speed in a variety of sports and in visual-spatial ability (Manning & Taylor, 2001; Manning, 2002a, 2002b). More male-like digit ratios

are also associated with deleterious traits such as increased rates of autism, immune deficiency and reduced verbal fluency (Manning, 2002a).

Austin et al. (2002) have suggested that any cognitive or personality trait which is influenced by prenatal testosterone and shows differences between the sexes will also correlate with digit ratio within each sex. Aggression is a sexually dimorphic trait. Men score higher than women on the physical, verbal, and hostility (but not anger) subscales of an aggression questionnaire (Buss & Perry, 1992). We examined the relationship between 2D:4D and scores on the four subscales of the aggression questionnaire. We hypothesized that testosterone organizes human aggressive behavior and that digit ratio will correlate with the most sexually dimorphic forms of trait aggression.

Methods

We tested 298 introductory psychology students (149 male and 149 female; median age 19) who participated for course credit. Participants completed a questionnaire and we made digital images of their hands. The study was approved by the University's human research ethics board and subjects participated only after giving their informed consent.

The questionnaire included Buss and Perry's (1992) aggression questionnaire and the Paulhus Deception Scale (PDS; see appendix). The aggression questionnaire consists of four sub-scales: hostility (8 questions), anger (7 questions), verbal aggression (5 questions), and physical aggression (9 questions). The PDS measures the tendency to give socially desirable responses and is divided into two sections: self-deception management (20 questions) and impression management (20 questions). Both tests used a one (extremely uncharacteristic of me) to five (extremely characteristic of me) Likert

scale. Questions from the different tests were combined and randomized so that no two questions from a section were placed together. If any of the questions in a particular category were left unanswered the participant was assigned a missing value for that category. Because Buss & Perry (1992) found that only some subscales of aggression were sexually dimorphic, we were interested in the properties of each subscale and ignored "total aggression", the sum of the four scales.

We dropped six male and seven female participants who scored high on the self deception or impression management scales. We did not attempt to partial out the effect of impression management or self-deception, but simply discarded those with high deception scores. The test scoring standards define high scores as greater than 7 for self-deception and greater than 14 for impression management. These thresholds correspond roughly to two standard deviations above the general population mean. Not knowing how our population compared to the general population, we applied the recommended absolute thresholds of 7 and 14 rather than those in the top two standard deviations of our sample.

Scanning was conducted prior to examining or analyzing questionnaire scores. A Hewlett Packard Scan-jet 5400C was used to scan participants' hands. Before scanning, small marks were drawn on the basal creases of the index and ring fingers using a ballpoint pen, by the first author. This was done to increase accuracy because it was difficult to see the creases clearly on the scans. Both of the participants' hands were scanned at the same time, palms down. Participants' index (2D) and ring (4D) fingers were measured from the hand scans using the GNU Image Manipulation Program (GIMP). The total length of each digit in units of pixels, from the middle of the basal

crease to the tip of the finger, was determined using the GIMP "measure" tool. The first author took all of the measurements. Ratios were calculated by dividing the length, in pixels, of the second digit (index finger) by the length, in pixels, of the fourth digit (ring finger) for both hands. This technique provides good reliability ($r = 0.98$, $df = 8$, $p < 0.01$ blind test-retest of ten individuals each scanned twice, with one week between the two scans).

We found stronger sexual dimorphism in digit ratio on the right hand than the left (as have many other authors, see above) and therefore present results for the right hand only.

We followed Moser and Stevens (1992) and employed the robust Welch's corrected t-test (the power cost is negligible and the potential benefit in rejecting false positives is high, even when data are not significantly heteroscedastic).

Results

Men had smaller finger length ratios than women (Table 2-1). Hostility, verbal, physical, and total aggression scores showed significant sexual dimorphism, while anger did not.

Anger significantly correlated with the other three sub-scales of aggression (hostility, verbal, and physical aggression) in men (Table 2-2). Of the other sub-scales, the two instrumental measures of aggression (verbal and physical) were correlated. All scores on the four sub-scales were correlated in women, except in the case of verbal aggression and hostility.

We determined the unique relationship between digit ratio and the four subscales of aggression using multiple regression. The regressions are presented in ANOVA table

format, along with the corresponding partial regression coefficients (Table 2-3). Males with lower finger length ratios had significantly higher physical aggression scores (partial regression plotted in Fig. 2-1). Finger length ratio did not predict anger, hostility, or verbal aggression in men. Female finger length ratio did not correlate with physical aggression, anger, hostility or verbal aggression.

Discussion

We found significant sexual dimorphism in physical aggression, verbal aggression, and hostility but no difference in anger. Physical aggression was the most sexually dimorphic of the aggression indices ($d = 1.05$). These results agree with Buss and Perry (1992), who found hostility, verbal, and physical aggression, but not anger to be sexually dimorphic, and trait physical aggression to be most dimorphic ($d = 0.89$).

We found digit ratio to correlate with physical aggression, but not with hostility, anger, or verbal aggression in males. There was no correlation between digit ratio and any measure of aggression in females. Our finding of a correlation between finger length ratio and physical aggression is as predicted by Austin et al. (2002). That they found no such result themselves- nor any correlation between finger length ratio and hostility or verbal aggression- may have been due to their use of an unusual sample, in which no reliable sex difference in digit ratio was found.

The results we have presented are consistent with the hypothesis that digit ratio reflects the organizational activity of androgens, and that variation in organizational effects of androgens causes some variation in adult physical aggression, but not anger, hostility or verbal aggression. If this explanation is correct, we would expect digit ratio to correlate with physical aggression in women and we did not find such an effect. One

possible explanation for this is that physical aggression scores on the Buss and Perry aggression questionnaire have been found to be affected by the stage of the menstrual cycle in women (Ritter, 2003). Our lack of control for this effect, and the possible effects of birth control medications may explain the lack of a significant correlation in women, and deserves further investigation.

The size of the correlation between digit ratio and physical aggression seen in men in the present study (partial $r_{1.24} = -0.21$; uncorrected $r = -0.16$) is larger than the reported relationship between aggression and adult testosterone concentrations reported in meta-analyses ($r = 0.14$, Archer et al., 1998; Book et al., 2001). Archer et al. (1998) found no relationship between adult testosterone concentrations and any of the four components of aggression on the aggression questionnaire used in this study. It is possible that correlations between adult testosterone levels and behaviour may be stronger once digit ratio effects are controlled for.

In summary, our results imply that prenatal testosterone, as assayed by digit ratio, has a stronger effect on trait physical aggression than do adult testosterone levels. This conclusion is based in part on the assumption that digit ratios reflect organizational effects of androgens, and that a questionnaire assay of aggressiveness is valid. This questionnaire has been validated by demonstrating a correlation between aggression scores and penalty minutes earned for aggressive offenses over the course of an ice hockey season (Bushman & Wells, 1998). We are currently collecting data on University hockey players' penalties and digit ratio to confirm these results using a behavioral assay. Further studies of digit ratio and aggressive behavior promise to yield insights into the source of individual variation in aggressiveness.

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Table 2-1

Digit ratios and aggression scores by sex

	Male			***Female***			***d***	***t***	***p***
	mean	sd	N	Mean	Sd	N			
Digit ratio	0.947	0.029	136	0.965	0.026	137	0.66	-5.43	<0.001
Physical	24.45	7.41	140	17.54	5.59	141	1.05	8.82	<0.001
Verbal	15.56	3.41	140	14.39	3.47	141	0.34	2.85	0.005
Hostility	21.45	5.45	140	22.68	4.82	140	0.24	-2.00	0.05
Anger	17.55	5.06	140	16.94	4.81	139	0.12	1.04	0.30

Means, standard deviations, sample size, Cohen's d, Welch's t, and p values for sexual dimorphism in digit ratios and test scores.

Table 2-2

Correlations between aggression questionnaire subscales by sex

Males

	Physical Aggression	Verbal Aggression	Hostility
Physical	-----		
Verbal	0.37 (<0.001)	-----	
Hostility	0.08 (0.33)	0.17 (0.051)	-----
Anger	0.49 (<0.001)	0.43 (<0.001)	0.45 (<0.001)

Females

	Physical Aggression	Verbal Aggression	Hostility
Physical	-----		
Verbal	0.37 (<0.001)	-----	
Hostility	0.24 (0.004)	0.13 (0.13)	-----
Anger	0.47 (<0.001)	0.58 (<0.001)	0.40 (<0.001)

Pearson's r (and p values) for correlations between subscales on the Buss & Perry Aggression Questionnaire.

Table 2-3

Multiple regression of digit ratio against aggression subscales

Males

	Sum Sq	Df	$r_{partial}$	F	p
Physical	0.004144	1	-0.21	4.91	0.028
Hostility	0.001410	1	0.13	1.67	0.198
Verbal	0.000752	1	0.09	0.89	0.347
Anger	0.000108	1	0.02	0.13	0.721
Error	0.108882	129			

Females

	Sum Sq	Df	$r_{partial}$	F	p
Hostility	0.000644	1	-0.10	1.05	0.308
Physical	0.000112	1	-0.03	0.18	0.670
Anger	0.000049	1	0.02	0.08	0.778
Verbal	0.000013	1	0.07	0.02	0.887
Error	0.076096	124			

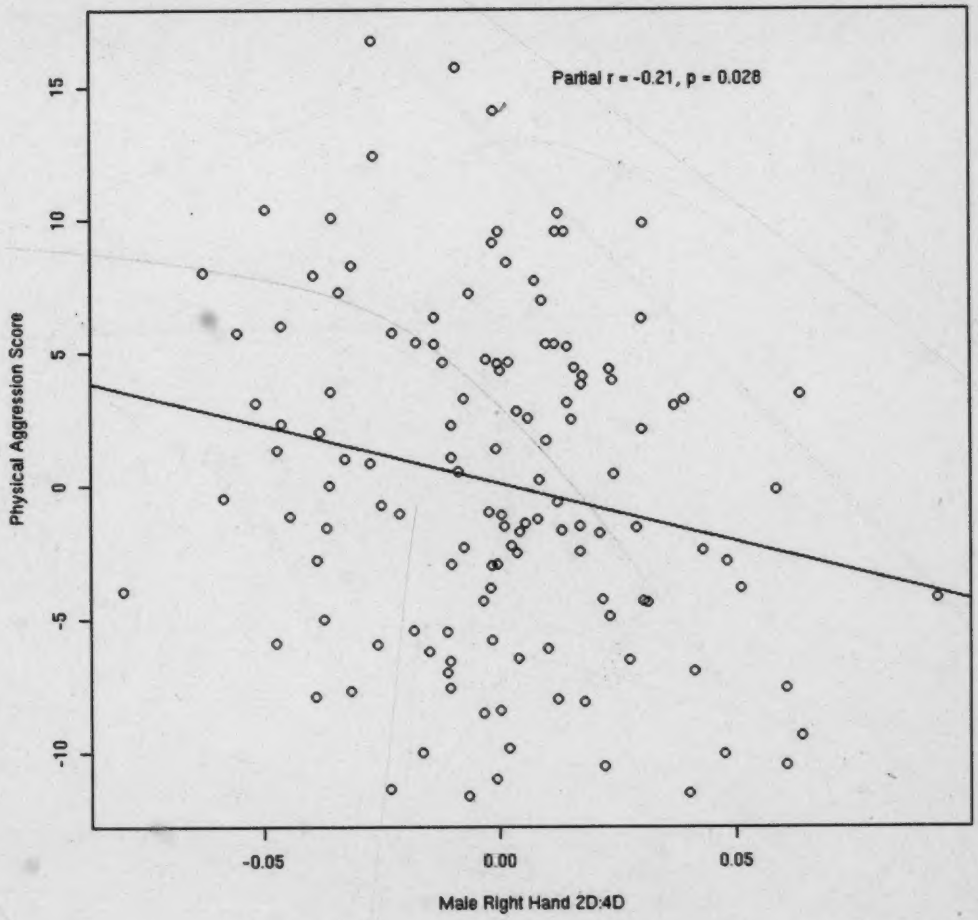

Figure 2-1. Unique relationship between male right hand finger length ratio (2D:4D) and physical aggression scores.

CHAPTER 3

Depression in Men is Associated with More Feminine Finger Length Ratios

Allison A. Bailey and Peter L. Hurd

In press *Personality and Individuals Differences*

Finger length ratio (2D:4D, index to ring finger) is a sexually dimorphic trait found in a variety of species ranging from humans and mice to zebra finches (Brown et al., 2002a; Burley & Foster, 2004; Manning, 2002a; Manning et al., 2000; Peters et al., 2002). On average, males have lower ratios (relatively shorter index (2D) fingers compared to ring (4D) fingers) than females. These digit ratios are thought to be fixed sometime during fetal development and to remain stable thereafter (Garn et al., 1975; Manning, 2002a; Manning et al., 1998).

Finger length ratio is becoming a widely used measure of prenatal testosterone (Manning, 2002a; Manning et al., 2003). Evidence in support of this view comes from digit ratio studies of individuals with congenital adrenal hyperplasia (CAH). Individuals (both male and female) with elevated fetal androgens due to CAH exhibit lower, more masculine, finger length ratios than controls (Brown et al. 2002b; Okten et al., 2002; but see Buck et al., 2003). Two causal mechanisms have been conjectured to explain this phenomenon. The first is that common genes (*Hoxa* and *Hoxd*) underlie the development of both digits and gonads (Kondo et al., 1997; Peichel et al., 1997) such that the timing of gene regulation leaves a finger length ratio that reflects the quantity of androgen produced. The second proposed mechanism is that finger length ratio is a function of androgen sensitivity, rather than androgen concentration. Lower finger length ratios are associated with androgen receptor alleles with fewer terminal domain CAG repeats in men (Manning et al., 2003), and fewer repeats produce receptors with higher androgen sensitivity (Chamberlain et al., 1994; Kazemi-Esfarjani et al., 1995).

Austin et al. (2002) have suggested that any sexually dimorphic personality trait influenced by prenatal testosterone will correlate with finger length ratio within each sex.

Manning and colleagues found significant correlations in men between lower, more masculine digit ratios and achievement, ability, and speed in a variety of sports and in visual-spatial ability (Manning & Taylor, 2001; Manning, 2002a, 2002b). Women with lower digit ratios reported higher, more masculinized scores on the Bem Sex Role Inventory (Csatho et al., 2003a). A number of previous studies have shown that men with more masculine finger length ratios tended to score higher on questionnaire-based tests of physical aggression (Bailey & Hurd, 2005), were perceived as being more masculine and dominant by female observers (Neave et al., 2003), and were more likely to show increased rates of autism and reduced verbal fluency (Manning, 2002a).

Depression is a sexually dimorphic trait (Endler et al., 2000, 2003). The risk and prevalence of major depression is about twice as high for females compared to males (Blazer et al., 1994; Piccinelli & Wilkinson, 2000; Rohr, 2002). Not only do women report depression more often, but they also report more symptoms per depressive episode, and are more susceptible to stressors than men (Sowa & Lustman, 1984; Wilhelm et al., 1998). According to Austin et al. (2002), higher, more feminine digit ratios should correlate with higher scores for depression within each sex.

Martin et al. (1999) suggested however, that increased risk of depression is a cost of high organizational testosterone. They found a negative, non-significant ($p = 0.24$), trend between 2D:4D and the severity of clinical depression in men, which has lead some authors (e.g. Csathó et al., 2003b) to mistakenly conclude that "…lower 2D:4D ratios are associated with […] depression (Martin, Manning, & Dowrick, 1999)". Manning (2002a) suggested further investigations were required to explain the non-significant results of earlier studies attempting to link digit ratio and depression. If early developmental

hormones affect depression, they should influence a stable part of the personality more than they affect fluctuating emotional states experienced in adulthood (such as depth of clinical depression). We measured depression using the NEO-PI depression sub-scale, which measures depression as a stable personality trait. We hypothesized that depression would correlate with 2D:4D on the right hand, such that individuals within sexes with more feminine finger length ratios would score higher on the NEO-PI depression sub-scale. Our prediction is in the opposite direction to the trend reported by Martin et al. (1999).

Methods

We tested 298 introductory psychology students (149 male and 149 female; median age 19; same participants used in chapter 2) who participated for course credit. After giving informed consent, participants had digital images of their hands made and completed a questionnaire, which included the NEO-PI trait depression sub-scale. The depression sub-scale is an eight-item questionnaire that uses a one (extremely uncharacteristic of me) to five (extremely characteristic of me) Likert scale to measure depression as a personality trait.

Scanning was conducted prior to examining or analyzing questionnaire scores. A Hewlett Packard Scan-jet 5400C was used to scan participants' hands. Before scanning, small marks were drawn on the basal creases of the index and ring fingers using a ballpoint pen by the first author. These marks increased measurement accuracy, as it was difficult to see the creases clearly on the scans without them. Both of the participants' hands were scanned at the same time, palms down. Participants' index (2D) and ring (4D) fingers were measured from the hand scans using the GNU Image Manipulation Program

(GIMP) measure tool. The total length of each digit was measured, in pixels, from the middle of the basal crease to the tip of the finger. Ratios were calculated by dividing the length of the second digit (index finger) by the length of the fourth digit (ring finger) for both hands. This measurement technique provides good reliability (blind test-retest of ten individuals each scanned twice, with one week between the two scans $r = 0.98$, $df = 8$, $p < 0.01$).

We used Pearson's r to correlate depression scores with right hand 2D:4D and Welch's corrected t-test to test for sexual dimorphism in 2D:4D. We followed Moser and Stevens (1992) and employed the robust Welch's corrected t-test as a matter of policy - the power cost is negligible and the potential benefit in rejecting false positives is high, even when data are not significantly heteroscedastic. All statistical tests were two-tailed.

Several authors have suggested that androgenization affects the right hand more than the left (Brown et al., 2002a; McFadden & Schubel, 2002; Williams et al., 2000). Digit ratio has consistently been shown to be more strongly differentiated on the right hand than on the left, in humans (Brown et al., 2002b; Lippa, 2003; Manning et al., 1998; McFadden & Schubel, 2002; Williams et al., 2000), regardless of handedness (Williams et al., 2000), and in mice (Brown et al. 2002a) and finches (Burley & Foster, 2004). Personality and behavioral traits have also been found to correlate more strongly with right hand digit ratio than left (Csatho et al., 2003a; Williams et al., 2000; Williams et al., 2003). For this reason, we present only right hand data.

Results

Men had smaller finger length ratios than women (male: 0.947, SD = 0.029, female: 0.965, SD = 0.026, $t_{277.45} = -5.49$, $p < 0.001$, $d = 0.65$). We found no sex

difference in depression scores (male: 21.90, SD = 5.46, female: 22.36, SD = 5.60, $t_{293.80}$ = -0.72, p = 0.475). Males with lower finger length ratios had lower trait depression scores than men with more feminine ratios (r_{139} = 0.17, p = 0.04; Figure 3-1). We found no such relationship in women (r_{139} = 0.02, p = 0.83).

Discussion

This is the first study to find a relationship between finger length ratio (2D:4D) and depression. We found higher levels of depression (measured as a personality trait) in males with higher, more feminine finger length ratios, suggesting that depression is associated with lower prenatal testosterone in men. Our results appear to contradict Martin et al. (1999) who reported a positive, but non-significant, relationship between prenatal testosterone (assayed by digit patterns) and depression in men. Austin et al. (2002) also failed to find a significant relationship between severity of depression and finger length ratio. Three possible explanations for discrepancies between the studies were differences in 1) statistical power, 2) depression assays, and 3) sample populations. First, the sample size in the present study was three times that used by Martin et al. (1999), and approximately twice that used by Austin et al. (2002). This suggests that the present study had more statistical power.

Secondly, tests measuring the severity of depression, such as the Beck Depression Inventory and Zung Self-Rating Depression Scale used by Martin et al. (1999) and Austin et al. (2002), were designed to diagnose clinical depression. It has been suggested that these tests may not be able to detect small differences in non-clinical populations (Krohne et al., 2002). Both state and trait depression are sexually dimorphic and correlate with one another (Endler et al., 2003). Therefore, depression as an underlying, stable trait

should influence adult state depression. If this is the case, then trait depression measures may be more sensitive to individual differences, and would more likely be influenced by prenatal testosterone.

Thirdly, Martin et al. (1999) used a mixed sample from both clinical and general populations to increase variability in depression severity scores. That we found no significant sexual dimorphism in depression scores may be due to an under-representation of depression in the university undergraduate population. A recent study using the same population found a very small, but statistically significant sex difference in depression (effect size = 0.003, n = 1800; P. Lee & N. Brown, personal communication). Such an effect would be difficult to detect in a sample as small as ours (n ~ 300). Williams et al. (2003) did not find emotionality in preschool children to be sexually dimorphic; the emotionality questions on their questionnaire were similar to items on our depression personality questionnaire. Austin et al. (2002) used university students and may have had a sample comparable to our own; however, they were unable to detect a sex difference in 2D:4D. They may have been unable to detect a relationship between depression and 2D:4D due to a limited amount of variation in 2D:4D as well as using a state depression assay on a non-clinical population.

We found no correlation between finger length ratio and depression in women. This finding follows all previous studies' findings. Williams et al. (2003) found that emotionality was not related to digit ratio in females, but was significantly, positively correlated with digit ratio in males (i.e. more feminine digit ratios, higher emotionality). Neither of the previous studies examining finger length ratio and clinical depression found even a hint of an association between digit ratio and depression in women (Austin,

et al., 2002; Martin et al., 1999). If male digit ratio correlates with sexually dimorphic psychological traits due to these both varying with the strength of defeminization, then a lack of a correlation in women may be ascribed to the lack of a defeminizing gonadal androgen exposure. We do not believe this to be the case, since digit ratio does correlate with sexually dimorphic psychological traits, at least in some cases (e.g. Benderlioglu & Nelson, 2004; Csathó et al 2003a, 2003b) perhaps reflecting the strength of adrenal source androgen exposure. Circulating hormone levels, including testosterone, which vary across menstrual phase have been demonstrated to influence depression scores; for example both high and low levels of testosterone are associated with increased depression (Chrisiansen 2001; Hartmann, et al 1996; Payne, 2003; Rohr, 2002). The organizational effects of androgens on trait depression, which we expect to see reflected in digit ratios, may therefore be concealed by the uncontrolled effects of menstrual cycles and/or birth control medication. Future studies should control for this variability when examining the relationship between behavior and finger length ratio in women. Previous investigations of digit ratio have found no correlation between digit ratio and the second-order trait of neuroticism (Austin, et al., 2002). There is some evidence that different genes are involved in linking neuroticism to major depression in men and women (Fanous, et al 2002). Larger samples of women than were used in the present study will be required to investigate the link between organizational androgens, circulating hormones, and the various components of neuroticism.

A variety of factors including experience, coping skills, and gonadal or stress hormones, are speculated to be the cause of the gender differences seen in depression (Martin et al., 1999; Nolan-Hoeksema, 1990; Piccinelli & Wilkinson, 2000; Rohr, 2002).

Many feel that "biological explanations of sex differences in depression have not been well supported" (Nolan-Hoeksema, 1990). Our results suggest that hormones prior to birth may organize a small, but statistically significant, difference in depression as a personality trait in males. This conclusion is subject to the caveats; 1) that we found no correlation between digit ratio and depression in women and 2) that the effect-size was small. Further research investigating the relationship between both state and trait depression with respect to digit ratio and prenatal androgens is clearly warranted.

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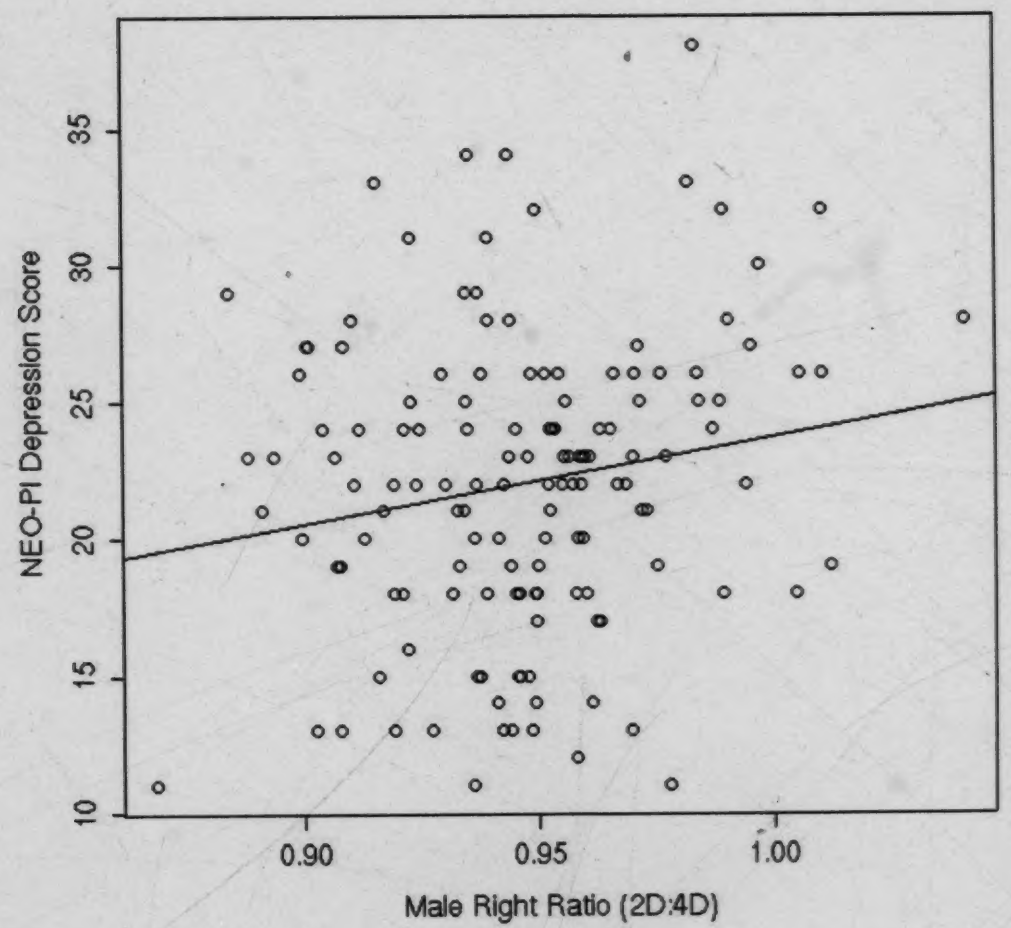

Figure 3-1. A significant positive correlation between right hand finger length ratio and NEO-PI trait depression sub-scale scores in men ($r_{139} = 0.17$, $p = 0.04$).

CHAPTER 4

Digit ratio (2D:4D) and behavioral differences between inbred mouse strains

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In press *Genes, Brain, and Behavior*

Many species show sexual differentiation in the ratio of second digit (index finger) to fourth digit (ring finger). In humans, males typically have smaller finger length ratios (i.e. shorter index fingers than ring fingers) than females (Manning, 2002a; Manning et al., 2000; Peters et al., 2002). Hand bone proportions are fixed in utero and digit ratio (2D:4D) is thought to remain stable during development (Brown et al., 2002a; Garn et al., 1975; Manning, 2002a; Manning et al., 1998).

Variation in digit ratio appears to be influenced by prenatal testosterone during development (Manning, 2002a; Manning et al., 2003a). Humans (both male and female) with elevated fetal androgens due to congenital adrenal hyperplasia exhibit lower, more masculine, finger length ratios than controls (Brown et al., 2002b; Okten et al., 2002). Two causal mechanisms have been conjectured to explain this phenomenon. The first is that common genes (*Hoxa* and *Hoxd*) underlie the development of both digits and gonads (Kondo et al., 1997; Peichel et al., 1997) such that the timing of gene regulation leaves a digit ratio that reflects the quantity of androgen produced. The second proposed mechanism is that finger length ratio is a function of androgen sensitivity, rather than androgen concentration. Androgen receptor alleles with fewer terminal domain CAG repeats produce receptors with higher androgen sensitivity (Chamberlain et al., 1994; Kazemi-Esfarjani et al., 1995) and are associated with lower finger length ratios (Manning et al., 2003a).

Hind paws in laboratory mice have also been found to follow the same sexually differentiated pattern as human hands (Brown et al., 2002a; Manning et al., 2003b). Inbred mouse strains are valuable models for investigating the causes of individual variation in behavior (Flint, 2003; Wahlsten et al., 2003). Considerable variation exists

between strains in behavior. Since each strain is genetically uniform, variation within strains is due to environmental -or gene by environment interaction- effects. The purpose of the present study was to test for variation in digit ratio across a number of inbred strains to assess the potential of inbred mouse strains for exploring organizational effects of sex hormones on behavioral traits.

Methods

Subjects were 184 male and female adult mice (~14-16 weeks old) from eight inbred strains. These mice were all euthanised at the conclusion of an unrelated study in accordance with all applicable laws and guidelines and as approved by the University of Alberta's Biological Sciences Animal Services' ethics review committee. All individuals were purchased from the same supplier (The Jackson Laboratory, Bar Harbor, ME), and were all subjected to the same housing, conditions, and tests prior to sacrifice. The strains and the sample sizes per sex were: 129S1/SvImJ (12 male, 11 female), A/J (12 male, 11 female), BTBR +T tf/tf (12 male, 11 female), BALB/cByJ (11 male, 12 female), C3H/HeJ (12 male, 11 female), C57BL/6J (12 male, 12 female), DBA/2J (11 male, 12 female) and FVB/NJ (11 male, 12 female). All paws were removed after euthanasia and preserved in a 10% formalin solution.

Paws were placed palm up and stuck to a piece of adhesive backing to ensure digits were completely flat. We chose this method because it was more effective than pressing the paws with a glass slide, which created a reflection, obscured paw details, and did not completely flatten the digits. Paws were photographed under a Wild M3Z stereoscope (Leica) with a Cohu 4815 video camera (Cohu, San Diego, CA) using an 8-bit gray scale. The software package, Global Laboratory Imaging, was used to capture,

sharpen, and save images for later analysis. The first sharpening filter was applied to all images. The GNU Image Manipulation Program (GIMP) measure tool was used to measure all images. All left paw images were digitally translated along the vertical axis to appear as right paws. Images were assigned random identifiers so as to render the scorers blind to individual, strain, or paw side. The length, in pixels, of the 2D and 4D for each paw was measured from the mid-point of the basal crease to the tip of the digit, excluding the nail (Figure 4-1). Digit ratios were calculated by dividing the length of the second digit (2D) by the length of the fourth digit (4D). The advantage of this method of digit measurement, from the basal crease rather than from a pin pressed into the V between digits as in Brown et al (2002a), was that the depth of the webbing between digits appeared to vary considerably between strains, but the basal crease did not seem to vary in its location on the paw. Also, measuring in pixels on a digital image avoided having to estimate tenths of a millimeter on a plastic ruler, as was necessary in Brown et al (2002a). Manning et al. (2003b) did not publish the methods used to obtain their data.

Images were divided equally and randomly between two scorers for measurement. We tested the inter-rater reliability of our technique on a set of ten randomly selected hind paws. The inter-rater reliability between two scorers' measures for rear 2D:4D was highly significant ($r=0.92$ $df=8$, $p<0.001$).

We used a 2-way between subjects ANOVA to analyze differences in digit ratio in the right rear paws, left rear paws, and the difference between the right and left paws between strains and sexes. A Pearson's r was used to examine the association between mean strain 2D:4D and sex differences of 2D:4D with the strain. Cohen's d (1988) was

used to estimate effect sizes for strain and sex effects. Cohen's d represents the difference between two group means divided by the pooled standard deviation.

Results

Digit ratios differed significantly between the strains on the right ($F_{7,168}$= 6.01, p < 0.001) and left ($F_{7,167}$ = 4.80, p< 0.001) rear paws (Figure 4-2). We found no difference in digit ratio between the sexes across strains (right: $F_{1,168}$= 0.07, p= 0.79; left: $F_{1,167}$= 0.14, p= 0.71) or a strain by sex interaction (right: $F_{7,168}$= 0.57, p= 0.78; left: $F_{7,167}$= 0.89, p= 0.52). There was a non-significant trend of positive association between mean strain 2D:4D and the direction and magnitude of the sex differences in digit ratio within strains (r_7 = 0.62, p =0.098). In other words, strains with higher digit ratios tended to have higher male digit ratios compared to female ratios, whereas strains with lower pooled digit ratios tended to have lower male digit ratios than female ratios. There was no relationship between digit ratio asymmetry (right ratio minus left ratio) and sex ($F_{1,167}$= 0.21, p=0.65), strain ($F_{7,167}$=0.59, p= 0.76), or a sex by strain interaction ($F_{7,167}$= 0.72, p= 0.65).

The effect sizes for sex differences were small (d'=0.023), even when strain effects were removed (d'=0.041). In comparison, the effect size of the difference between DBA/2J and C3H/HeJ mice was large, d'=1.460. A non-parametric bootstrap based on 1000 resamplings (Efron & Tibshirani, 1993) was used to calculate a 95% confidence interval on the magnitude of the sex effect. The ratio of male to female scores for the right rear paws has a 95%CI of 0.987 to 1.015. When strain differences are partialled out, the 95%CI on ratio of male to female scores was 0.989 to 1.015, the 95% confidence interval on the effect size for sex was d' = -0.25 to 0.32.

Discussion

Digit ratios differed significantly between the inbred strains, but not between the sexes. We also found no significant differences between sexes or strains in the lateral asymmetry in digit ratios. No such sex effect on digit ratio asymmetry exists in humans (Putz et al., 2004). The failure to find an overall sex effect is surprising. Brown et al. (2002a) found digit ratio to be sexually differentiated in the right rear paw only of outbred laboratory mice, whereas Manning et al. (2003b) found only the left rear paw to be sexually differentiated. We believe the sex effects found in these earlier studies to be real. Possible explanations for these different results include 1) different methods used to measure digit length, 2) different effective sample sizes, and 3) different types of mice were used.

Our scores cannot be compared directly to either previous study because of the different measuring methods used, but we do not believe that the difference in methods is the source of the difference in results. We estimated the effect size of sex from Brown et al. (2002a) to be d'=0.357. This is larger than the 95% confidence interval for the sex effect calculated from our data, but not nearly as large as the effect sizes found between the most different strains in our study. This suggests that we had enough power to detect a sex effect had there been one. We found no clear trend in digit ratio between the sexes, such that a larger sample size in our study would have produced a sex effect. We believe the reason we did not find a net sex effect is that this effect varies between strains. Strains with higher digit ratios tended to have sex effects in the opposite direction from strains with lower digit ratios. The small number of mice per strain may have provided insufficient power to detect a sex by strain interaction. Alternatively, inbreeding may

somehow disrupt the sex differences in digit ratio.

Intra-uterine position (Clark & Galef, 1995; vom Saal & Bronson, 1980) may also contribute variability to digit ratios, masking the effect of sex. Pups that gestate between two males may have different digit ratios than those that gestate between two females. Interstrain variation in litter size may also contribute to IUP effects on mean strain digit ratio. There was no obvious correlation between mean litter size per strain, or average sex ratio at weaning (data from mpd149.dat, the Mouse Phenome Database, q.v.) with either mean strain digit ratio, or mean female digit ratio. However, only four strains used in our study also appear in the reproductive performance data set. Further research is warranted into the relationship between digit ratio, IUP, and inter-strain variation.

We identified a number of traits in the Mouse Phenome Database (http://www.jax.org/phenome) to assess the potential of using inbred mice for investigating the association between digit ratio and behavioral traits thought to be influenced by developmental androgens. The mouse behavioral traits we chose seemed to correspond to human behavioral traits, which have been shown to correlate with digit ratio in previous studies. Some of these assays may not model the human traits well, and caution is warranted in interpreting the results. Table 4-1 lists the behavioral mice traits, the corresponding human traits, and the correlation found between mean mice traits and the mean right rear digit ratios for each sex and strain combination in this study. As each of the mouse traits measured showed a strong trend, significant effect of sex, or sex by strain interaction in the data sets used (sex effect: total daily activity $p<0.001$, blood pressure $p<0.051$, body weight $p<0.001$; interaction: number of bites $p<0.06$), we analyzed each strain by sex mean as a separate datum. Although our eight strains

produced fairly low statistical power, table 4-1 shows a general tendency for those traits to correlate with digit ratio.

We chose to analyze the relationships between behavioral data and the right rear paw because several authors have suggested that androgenization affects the right hand more than the left (Brown et al., 2002a; McFadden & Schubel, 2002; Williams et al., 2000). Digit ratio has consistently been shown to be more strongly differentiated on the right hand than on the left, in humans (Brown et al., 2002b; Lippa, 2003; Manning et al., 1998; McFadden & Schubel, 2002; Williams et al., 2000), regardless of handedness (Williams et al., 2000), and in mice (Brown et al., 2002a), and finches (Burley & Foster, 2004). Personality and behavioral traits also correlate more strongly with right hand digit ratio than left (Csatho et al., 2003a, 2003b; Williams et al., 2000; Williams et al., 2003).

It is difficult to interpret the results summarized in Table 4-1 without wondering whether smaller or larger ratios are the more masculine in mice. In humans, not only is there a sex difference in digit ratio, but behavioral variation also correlates with digit ratio within sexes consistently with the sexual variation in that behavior. Mice strains did not show such a simple effect. Higher ratios in mice hind feet were associated with more masculine behavioral traits such as increased aggression, and increased activity. These effects are the opposite to that of previous studies with human hand digit ratios. Lower digit ratio in humans tends to correlate with more masculine traits such as increased physical aggression and increased speed, ability, and achievement in sports (Bailey & Hurd, 2005; Manning, 2002a, 2002b; Manning & Taylor, 2001). In humans and two strains of mice, the average male digit ratio is lower than the average female digit ratio; however, foot digit ratio in humans and zebra finches shows reverse sexual

differentiation (i.e. females have smaller ratios than males; Burley & Foster, 2004; McFadden & Schubel, 2002; Manning et al. 2003b).

The current findings show promise for investigating the relationship between developmental androgens, digit ratio, and behavioral traits. Inbred mice strains appear to provide large stable differences in baseline digit ratios. More research needs to be done both to elucidate the sex effect within strains, and to correlate digit ratio with other morphological correlates of androgenization such as anogenital distance.

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Table 4-1

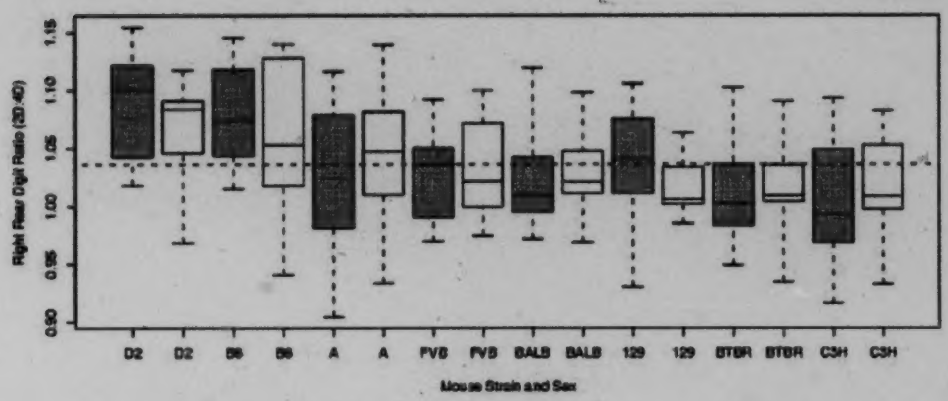
The relationship between average inbred mouse strain digit ratios and behavioral traits compared with the existing digit ratio-behavioral trait relationships in humans.

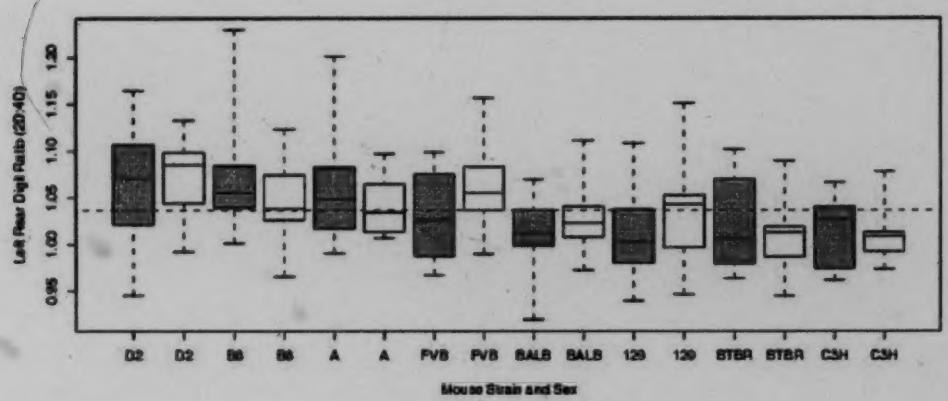
	Inbred Mice				Humans
Trait Measured	Digit Ratio-Trait Correlation			Interpretation	Existing Digit Ratio-Trait Relationship
	R	df	P		
Activity[a] –total daily activity	0.52	12	0.058	Higher ratios-> trend towards increased activity	Lower ratios-> increased speed, achievement, and ability in sports (Manning & Taylor, 2001)
Aggression[b] - average number of bites	0.65	14	0.006	Higher ratios-> increased aggression	Lower ratios-> increased physical aggression (Bailey & Hurd, 2005)
Anxiety[c] - % of time in open quadrants	-0.45	12	0.11	Lower ratios-> trend towards more anxiety exhibited	Higher ratios-> more trait depression exhibited (Bailey & Hurd, in press)
Systolic blood pressure[d]	0.52	12	0.055	Higher ratios -> trend towards increased systolic blood pressure	Lower ratios-> myocardial infarction happens later in life (Manning & Bundred, 2001)
Body weight[e]	-0.24	14	0.36	No relationship	No relationship (Manning et al., 2000b)

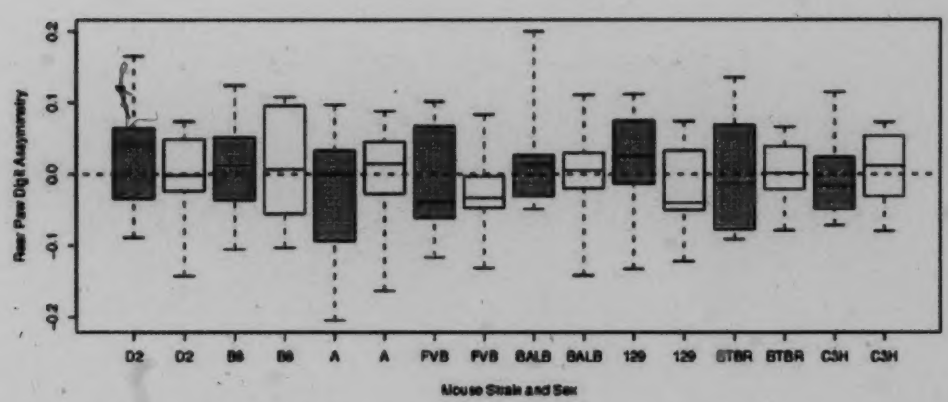
Note. Mice behavioral data for each strain were obtained from http://www.jax.org/phenome. The data sets (trait abbreviations in data sets) used were: [a]MPD:92 (tot_daily), [b]MPD:160 (nbite), [c]MPD:118 (pct_open), [d]MPD:104 (BP), [e]MPD108 (bw). The correlations are between the average right rear digit ratios for males and females within each of the eight strains and the strain average for each behavioral trait.

Figure 4-1. Photograph of the right rear paw palm from a female DBA/2J mouse illustrating the landmarks used to measure mice 2D:4D.

Figure 4-2. Digit ratio for eight inbred mice strains by sex in right rear paws (top), left rear paws (middle), and asymmetry between rear paws (bottom). Strains are DBA/2J (D2), C57BL/6J (B6), A/J (A), FVB/NJ (FVB), BALB/cByJ (BALB), 129S1/SvImJ (129), BTBR_+T_tf/tf (BTBR), and C3H/HeJ (C3H). Gray boxes denote male mice and white boxes denote female mice for each strain. Boxes indicate the first and third quartiles while the median is marked with a horizontal line, whiskers extend to the most extreme datum. The horizontal dotted lines represent the average digit ratio for all strains combine.


Right Rear Digit Ratio (2D:4D)
0.90
0.95
1.00
1.05
1.10
1.15
D2 D2 B6 B6 A A FVB FVB BALB BALB 129 129 BTBR BTBR C3H C3H
Mouse Strain and Sex


Left Rear Digit Ratio (2D:4D)
0.95
1.00
1.05
1.10
1.15
1.20
D2 D2 B6 B6 A A FVB FVB BALB BALB 129 129 BTBR BTBR C3H C3H
Mouse Strain and Sex


Rear Paw Digit Asymmetry
-0.2
-0.1
0.0
0.1
0.2
D2 D2 B6 B6 A A FVB FVB BALB BALB 129 129 BTBR BTBR C3H C3H
Mouse Strain and Sex

CHAPTER 5

Discussion

All three studies support the androgenization of trait dimorphism hypothesis and the ontogenetic influence of androgens on individual variation of personality traits in both humans and mice. This is the first time that aggression and depression have been shown to significantly correlate with digit ratio in men. These associations were expected based on the ATD hypothesis; however, previous studies have lacked the ability to find such associations (Austin et al., 2002; Martin et al., 1999). Support is also provided for extending the ATD hypothesis to rodent models, specifically with respect to digit ratio and aggression.

Physical aggression was found to negatively correlate with digit ratio in men. This result suggests that androgens organize adult aggressive behavior in human men much the same way as in male animal models (Crews et al., 1998; Moore et al., 1998; Ryan & Vandenbergh, 2002). We found no evidence; however, to support a relationship between organizational androgens and adult aggressive behavior in women. This result is counterintuitive given the organizational effect of androgens on reactive aggression in women (Benderlioglu & Nelson, 2004), and aggressive and reproductive behaviors in female gecko and rodent models (Crews et al., 1998; Ryan & Vandenbergh, 2002). As discussed earlier, a possible explanation for this discrepancy was the way aggression was assayed because answers to the questionnaire were activationally affected by hormones in women (Ritter, 2003). A more valid and convincing measure of human aggression requires a behavioral assay of aggression, such as penalty minutes for aggressive violations in hockey (Bushman & Wells, 1998). I have collected preliminary data that shows hockey players in defensive positions (traditionally more aggressive individuals) tend to have lower digit ratios (or higher exposure to prenatal testosterone) than forward

players (Unpublished data). In addition, male undergraduates that report more physical aggression also report having sex at an earlier age, with more partners, and are more likely to philander while in a serious relationship (Bailey & Hurd, in prep.). These results are consistent with the hypothesis that males employing alternative life history strategies differ in their digit ratios. I have found no evidence for such alternative strategies in women (Bailey & Hurd, in prep).

Similar to aggression, depression in men also followed the pattern predicted by the androgenization of trait dimorphism hypothesis. Men with more feminine finger ratios reported more depression, a personality trait that is more prevalent in women (Blazer et al., 1994; Piccinelli & Wilkinson, 2000; Rohr, 2002). Again, no organizational relationship was found between depression and digit ratio in women. I suspect that either the assay was not sensitive enough to detect variation in female depression or it was subject to activational fluctuations in hormone concentrations. An alternative hypothesis suggests that females either do not vary as much as males for particular personality and behavioral traits, or that these behaviors are not organized during development in the same manner as seen in some animal models. Future research should look at the relationship between trait depression, state depression, and digit ratio to test whether depression is in fact organized in females and confirm the demonstrated relationship between trait depression and digit ratio seen in the present study.

The third study shows a significant digit ratio dimorphism between strains, but not between the sexes within each strain. Similarly, ethnic differences in digit ratio are stronger than differences between the sexes in some human populations (Manning et al., 2003b). Sexual dimorphism in digit ratio has been consistently demonstrated across a

wide variety of human populations (Manning, 2002; Manning et al., 2000) and in two breeds of mice (Brown et al., 2002; Manning et al., 2003a). Given previous findings, I expected male mice to exhibit smaller, more masculine digit ratios on the hind paw compared with female mice in all eight inbred mice strains. Since no digit ratio sexual dimorphism was found in any of the strains, it was impossible to ascertain whether a smaller digit ratio in the hind paws of each strain was a masculine or feminine digit ratio. Larger digit ratios correlated with more masculine behavior (e.g. aggression), which suggests that inbred mice might exhibit reverse sexual dimorphism in the hind limbs, as seen in zebra finches and humans (Burley & Foster, 2004; McFadden & Schubel, 2002). One possible explanation for the lack of sexual dimorphism in inbred mice digit ratios was the small sample sizes of each sex within each strain. Another reason for the lack of digit ratio sexual dimorphism might have been due to intrauterine (IUP) position effects. Placement within the uterine horn causes considerable intrasex variation of developmental androgens (Ryan & Vandenbergh, 2002) that might mask sexual differentiation of digit ratio in inbred mice. I have recently collected data that shows 2M individuals of both sexes have larger digit ratios than 0M individuals (Hurd et al., submitted). Future studies with inbred strains should examine fewer strains with more individuals per sex and strain. This would help clarify whether sexual dimorphism exists and in which direction for inbred strains.

Compared with animal models, the strength of the relationship between developmental androgens (measured using digit ratio) and human personality traits is small. Digit ratio explained less than five percent of the variability seen in male aggression and depression. This smaller effect in human studies might be due to a

stronger, more easily detected organizational effect of androgens on behavior in animal models or the fewer number of traits in which animals differ as compared to humans. Animal personalities are commonly divided into dichotomies or artificially selected for in opposite directions along one dimension- territorial vs. non-territorial, slow vs. fast, bold vs. shy and so on, when in fact we might expect that natural selection would generate a more continuous variation in personality (Bakker, 1986; Groothuis & Carere, 2005). Therefore differences in personality might be larger between individuals differing for a dichotomous personality trait than individuals differing for a continuous variable in a smaller sample. An alternative explanation for the weaker relationship is that digit ratio might reflect variation in other developmental hormones instead of or in addition to prenatal testosterone. Preliminary data showed that maternal stress explained up to forty percent of the variation in offspring digit ratio, which suggested that digit ratios might reflect other hormones such as prenatal cortisol levels (Hurd et al., in prep). Future research using mice models could experimentally manipulate concentrations of different types of developmental hormones and the timing of these hormones to test which hormones permanently organize digit ratio, provided intra-sex androgen variations due to IUP effects are taken into account.

I have shown that digit ratio explains a small, but significant, amount of the variability seen in personality in both humans and mice. My findings are consistent with the idea that digit ratio is a good morphological measure of prenatal testosterone exposure and/or sensitivity, and that androgen exposure and/or sensitivity has a life-long influence on personality. Future research should examine the effects of a range of

hormones on digit ratio and behavior as a function of the stage of development at which they are administered.

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Appendix- Questionnaires used in Chapters 2 & 3

Reprinted from the Buss and Perry (1992) Aggression Questionnaire

Physical Aggression

1. Once in a while I can't control the urge to strike another person
2. Given enough provocation, I may hit another person
3. If somebody hits me, I hit them back
4. I get into fights a little more than the average person
5. If I have to resort to violence to protect my rights, I will
6. There are people who pushed my so far that we have come to blows
7. I can think of no good reason for ever hitting a person (*reversed question*)
8. I have become so mad that I have broken things
9. I have threatened people that I know

Verbal Aggression

1. I tell my friends openly when I disagree with them
2. I often find myself disagreeing with other people
3. When people annoy me, I may tell them what I think of them
4. I can't help getting into arguments when people disagree with me
5. My friends say that I'm somewhat argumentative

Anger

1. I flare up quickly, but get over it quickly
2. When frustrated, I let my irritation show
3. I sometimes feel like a powder keg ready to explode
4. I am an even-tempered person (*reversed question*)
5. Some of my friends think I'm a hothead
6. Sometimes I fly off the handle for no good reason
7. I have trouble controlling my temper

Hostility

1. I am sometimes eaten up with jealousy
2. At times I feel I have gotten a raw deal out of life
3. Other people always seem to get the breaks
4. I wonder why sometimes I feel so bitter about things
5. I know that "friends" talk about me behind my back
6. I am suspicious of overly friendly strangers
7. I sometimes feel that people are laughing at me behind my back
8. When people are especially nice, I wonder what they want

Reprinted from the NEO-PI depression sub-scale

1. I rarely feel lonely or blue (*reversed question*)
2. Sometimes I feel completely worthless
3. Too often, when things go wrong, I get discouraged and feel like giving up
4. I am seldom sad or blue (*reversed question*)
5. I have sometimes experienced a deep sense of guilt or sinfulness
6. I tend to blame myself when things go wrong
7. I have a low opinion of myself
8. Sometimes things look pretty bleak and hopeless to me

Reprinted from the Paulhus Self Deception Scales

Self Deception Management

1. My first impressions of people usually turn out to be right
2. It would be hard for me to break any of my bad habits
3. I don't care to know what other people really think of me
4. I have not always been honest with myself
5. I always know why I like things
6. When my emotions are aroused, it biases my thinking
7. Once I've made up my mind, other people cannot change my opinion
8. U an bit a safe driver when I exceed the speed limit
9. I am fully in control of my own fate
10. It's hard for me to shut off a disturbing thought
11. I never regret my decisions
12. I sometimes lose out on things because I can't make up my mind soon enough
13. The reason I vote is because my vote can make a difference
14. People don't seem to notice me and my abilities
15. I am a completely rational person
16. I rarely appreciate criticism
17. I am very confident of my judgements
18. I have sometimes doubted my ability as a lover
19. It's alright with me if some people happen to dislike me
20. I'm just an average person

Impression Management

1. I sometimes tell lies if I have to
2. I never cover up my mistakes
3. There have been occasions when I have taken advantage of someone
4. I never swear
5. I sometimes try to get even rather than forgive and forget
6. I always obey laws, even if I'm unlikely to get caught
7. I have said something bad about a friend behind his or her back
8. When I hear people talking privately, I avoid listening

9. I have received too much change from a salesperson without telling him or her
10. I always declare things at customs
11. When I was young, I sometimes stole things
12. I have never dropped litter on the street
13. I sometimes drive faster than the speed limit
14. I never read sexy books or magazines
15. I have done things that I don't tell other people about
16. I never take things that don't belong to me
17. I have taken sick leave from work or school even though I wasn't really sick
18. I have never damaged a library book or store merchandise without reporting it
19. I have some pretty awful habits
20. I don't gossip about other people's business

Note. All questionnaires used a one (extremely uncharacteristic of me) to five (extremely characteristic of me) Likert scale. Questions from the questionnaires were combined and randomized so that no two questions from a section were placed together. Physical aggression, verbal aggression, hostility, anger, and depression scores were calculated by adding the numerical response to each question within a particular category. For reversed questions, six was subtracted from the numerical response to obtain the correct score for that question. For the self deception and impression management questions, the scoring system provided by the writers of the test was used. On the self-deception scale, a participant scored one point for answering a 5 to the odd numbered questions and a one to the even numbered questions. On the impression management scale, a participant scored one point for answering a one or two to the odd numbered questions and a four or five to the even numbered questions. The test scoring standards define high scores as greater than seven for self-deception and greater than 14 for impression management.